

In claim 4, line 1, please delete "claim 1", and insert --claim 18-- in its place.

In claim 8, line 1, please delete "claim 1", and insert --claim 18-- in its place.

In claim 9, line 1, please delete "claim 1", and insert --claim 18-- in its place.

In claim 10, line 1, please delete "claim 1", and insert --claim 18-- in its place.

In claim 12, line 1, please delete "claim 1", and insert --claim 18-- in its place.

In claim 13, line 1, please delete "claim 1", and insert --claim 18-- in its place.

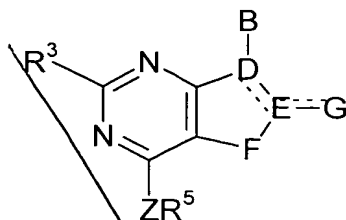
In claim 14, line 1, please delete "claim 1", and insert -- claim 18-- in its place.

Please amend claims 2, 3, 18, 20, and 21 as follows:

C¹
2. (Amended) A compound according to claim [1] 18 wherein: R¹ is C₁-C₆ alkyl, which may optionally be substituted with one hydroxy, fluoro, CF₃, or C₁-C₄ alkoxy group and may optionally contain one double or triple bond provided at least two carbons are present in the C₁-C₆ alkyl group; and R² is benzyl, C₁-C₆ alkyl, which may optionally contain one double or triple bond provided at least two carbons are present, wherein said C₁-C₆ alkyl and the phenyl moiety of said benzyl may optionally be substituted with one fluoro, CF₃, or C₁-C₂ alkyl, C₁-C₂ alkoxy or chloro group.

3. (Amended) A compound according to claim [1] 18 wherein: R³ is methyl, ethyl, chloro or methoxy; R⁴ is methyl, ethyl or trifluoromethyl; G is hydrogen, methyl, ethyl, or E=G is C=O or C=S; and R⁵ is phenyl, pyridyl, or pyrimidyl which is substituted with more than two substituents which are independently selected from C₁-C₄ alkyl and -O(C₁-C₄ alkyl), (C₁-C₄ alkyl)-O-(C₁-C₄ alkyl), CF₃, OCF₃, -CHO, (C₁-C₄ alkyl)-OH, CN, Cl, F, Br, I and NO₂, wherein one of the carbon-carbon single bonds of each of the foregoing (C₁-C₄)alkyl groups having at least two carbons may optionally [contain one] be replaced by a carbon-carbon double or triple bond.

C²
Sub
E'
18. (Amended) A compound of the formula



wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E, or D is CH and is single bonded to E;

F is oxygen, sulfur, CHR^4 or NR^4 when it is single bonded to E;

G, when single bonded to E, is hydrogen, C_1 - C_4 alkyl, $-S(C_1-C_4 \text{ alkyl})$, $-O(C_1-C_4 \text{ alkyl})$, NH_2 , $-NH(C_1-C_4 \text{ alkyl})$ or $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, wherein each of the C_1 - C_4 alkyl groups of G may optionally be substituted with one hydroxy, $-O(C_1-C_2 \text{ alkyl})$ or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

R^1 is hydrogen, C_1 - C_6 alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, CF_3 , $-C(=O)O(C_1-C_4 \text{ alkyl})$, $-OC(=O)(C_1-C_4 \text{ alkyl})$, $-OC(=O)N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-CN$, $-NO_2$, $-SO(C_1-C_4 \text{ alkyl})$, $-SO_2(C_1-C_4 \text{ alkyl})$, $-SO_2NH(C_1-C_4 \text{ alkyl})$ and $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, wherein [one or two of the] a carbon-carbon single [bonds] bond of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1 - C_4 alkyl groups in the foregoing R^1 groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1 - C_{12} alkyl wherein [from one to three of the] one carbon-carbon single [bonds] bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or R^2

C²
C¹
cont

is aryl or (C₁-C₄ alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R² is C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ² wherein Z² is selected from hydrogen, C₁-C₄ alkyl, benzyl and C₁-C₄ alkanoyl, and wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from bromo, iodo, C₁-C₆ alkoxy, -OC(=O)(C₁-C₆ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), amino, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)-CO-(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SH, -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl);

-NR¹R² or -CR¹R²R¹⁰ may form a saturated 3 to 8 membered ring that, in the case of -CR¹R²R¹⁰, is carbocyclic, and that, in the case of -NR¹R², contains a single heteroatom, nitrogen, which ring may optionally contain from one to three double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

R³ is hydrogen, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C₁-C₄ alkyl) or -SO₂(C₁-C₄ alkyl) wherein each of the (C₁-C₄ alkyl) moieties in the foregoing R³ groups may optionally be substituted with one substituent R⁹ selected from hydroxy, fluoro and (C₁-C₂ alkoxy);

each R⁴ is, independently, hydrogen, (C₁-C₆ alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, -O(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄)alkyl, -CO(C₁-C₄ alkyl), -C(=O)H or -C(=O)O(C₁-C₄alkyl), wherein one or two of the carbon-carbon single bonds in each of the (C₁-C₆ alkyl) and (C₁-C₄ alkyl) moieties in the foregoing R⁴ groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of these moieties may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C₁-C₃

alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH_3 , fluoro, chloro, $\text{C}_1\text{-C}_3$ alkylthio, -CN , -COOH , $\text{-C(=O)O(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-C(=O)(C}_1\text{-C}_4\text{ alkyl)}$ and -NO_2 ;

*C²
C¹
Cont*

R^5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, pyrimidyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or $\text{C}_3\text{-C}_8$ cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^4 wherein Z^4 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl or benzyl; and wherein each of the foregoing R^5 groups is substituted with from one to four substituents R^{12} wherein one to three of said substituents may be selected, independently, from chloro, $\text{C}_1\text{-C}_6$ alkyl and $\text{-O(C}_1\text{-C}_6\text{ alkyl)}$ and one of said substituents may be selected from $(\text{C}_1\text{-C}_4\text{ alkyl})\text{O(C}_1\text{-C}_4\text{ alkyl)}$, OCF_3 , fluoro, bromo, iodo, formyl, -CN , -CF_3 , -NO_2 , -NH_2 , $\text{-NH(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-N(C}_1\text{-C}_2\text{ alkyl)(C}_1\text{-C}_6\text{ alkyl)}$, $\text{-C(=O)O(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-C(=O)(C}_1\text{-C}_4\text{ alkyl)}$, -COOH , $\text{-SO}_2\text{NH(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-SO}_2\text{N(C}_1\text{-C}_2\text{ alkyl)(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-SO}_2\text{NH}_2$, $\text{-NHSO}_2\text{(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-S(C}_1\text{-C}_6\text{ alkyl)}$ and $\text{-SO}_2\text{(C}_1\text{-C}_6\text{ alkyl)}$, and wherein each of the $\text{C}_1\text{-C}_4$ alkyl and $\text{C}_1\text{-C}_6$ alkyl moieties in the foregoing R^5 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl, and wherein a carbon-carbon single bond of each of the $\text{C}_1\text{-C}_4$ alkyl and $\text{C}_1\text{-C}_6$ alkyl moieties in the foregoing R^5 groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond], and wherein when (a) R^3 is methyl, ethyl, chloro or methoxy, and (b) R^4 is methyl, ethyl or trifluoromethyl, and (c) either G is hydrogen, methyl, ethyl or E=G is C=O or C=S , and (d) R^5 is phenyl substituted with one or more $(\text{C}_1\text{-C}_4)\text{alkyl}$ groups then one of the carbon-carbon single bonds of each of said $(\text{C}_1\text{-C}_4)\text{alkyl}$ may optionally be replaced by a carbon-carbon double or triple bond];

R^7 is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, halo, cyano, hydroxy, $\text{-O(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-C(=O)(C}_1\text{-C}_4\text{ alkyl)}$, $\text{-C(=O)O(C}_1\text{-C}_4\text{ alkyl)}$, -OCF_3 , -CF_3 , $\text{-CH}_2\text{OH}$, $\text{-CH}_2\text{O(C}_1\text{-C}_4\text{ alkyl)}$;

R^{10} is hydrogen, hydroxy, methoxy or fluoro;

R^{11} is hydrogen or $\text{C}_1\text{-C}_4$ alkyl; and

with the proviso that: (a) when R^4 is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

C1
cont
C2

Z is NH, oxygen, sulfur, -N(C₁-C₄ alkyl), -NC(=O)(C₁-C₂ alkyl), NC(=O)O(C₁-C₂alkyl) or CR¹³R¹⁴ wherein R¹³ and R¹⁴ are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R¹³ and R¹⁴ can be cyano;

or a pharmaceutically acceptable salt of such compound.

C3
sub
C2

20. (Amended) A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, fibromyalgia, depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, [acquired immune deficiency syndrome (AIDS)] human immunodeficiency virus infections, Alzheimer's disease, Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, psychosocial dwarfism, and hypoglycemia in a mammal, comprising an amount of a compound according to claim [1] 18 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.

21. (Amended) A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, fibromyalgia, depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome,

C3
E2
Cont

Crohn's disease, spastic colon, [acquired immune deficiency syndrome (AIDS)] human immunodeficiency virus infections, Alzheimer's disease, Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim [1] 18, that is effective in treating such disorder.

Please add the following claims 22, 23, and 24:

C4

--22. A compound according to claim 18 wherein: R^4 is not trifluoromethyl; R^5 is not pyrimidyl; and R^{12} is not $(C_1-C_4 \text{ alkyl})O(C_1-C_4 \text{ alkyl})$, OCF_3 , or fluoro.--

sub
E3

--23. A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, fibromyalgia, depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, Alzheimer's disease, Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, psychosocial dwarfism, and

hypoglycemia in a mammal, comprising an amount of a compound according to claim 22 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.--

C4
C3
cont
--24. A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, fibromyalgia, depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthymia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, Alzheimer's disease, Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate antidiarrhetic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim 22, that is effective in treating such disorder.--

REMARKS

Applicant thanks the Examiner's for indicating that claim 19 is allowable, except for that it depends from a rejected claim.

Applicant has amended the claims above and presented remarks, supra, to overcome the rejections set forth in the March 26, 1998 Office Action. Reconsideration of this application is respectfully requested in light of these amendments and the following remarks.

In particular, applicant has amended claims 2, 3, and 18, and added claims 22, 23, and 24. Applicant has canceled claim 5 in response to the Examiner's noting that claim 5 was superfluous and did not further limit the claim from which it depends. Thus, upon entry of the